

10/513699

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\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	4	AUG 13	CA/CAPplus enhanced with additional kind codes for granted patents
NEWS	5	AUG 20	CA/CAPplus enhanced with CAS indexing in pre-1907 records
NEWS	6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	7	AUG 27	USPATOLD now available on STN
NEWS	8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	10	SEP 13	FORIS renamed to SOFIS
NEWS	11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	12	SEP 17	CA/CAPplus enhanced with printed CA page images from 1967-1998
NEWS	13	SEP 17	CAPplus coverage extended to include traditional medicine patents
NEWS	14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	15	OCT 02	CA/CAPplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	16	OCT 19	BEILSTEIN updated with new compounds
NEWS	17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	18	NOV 19	WPIX enhanced with XML display format
NEWS	19	NOV 30	ICSD reloaded with enhancements
NEWS	20	DEC 04	LINPADOCDB now available on STN
NEWS	21	DEC 14	BEILSTEIN pricing structure to change
NEWS	22	DEC 17	USPATOLD added to additional database clusters
NEWS	23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS	24	DEC 17	DGENE now includes more than 10 million sequences
NEWS	25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS	26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS	27	DEC 17	CA/CAPplus enhanced with new custom IPC display formats
NEWS	28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS	29	JAN 02	STN pricing information for 2008 now available
NEWS	30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	31	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new

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=> file casreact  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.46	0.67

FULL ESTIMATED COST

FILE 'CASREACT' ENTERED AT 11:52:10 ON 01 FEB 2008  
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT  
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FILE CONTENT:1840 - 26 Jan 2008 VOL 148 ISS 5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

\*\*\*\*\*  
\*  
\* CASREACT now has more than 13.8 million reactions \*  
\*  
\*\*\*\*\*

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

Uploading C:\Program Files\Stnexp\Queries\10524517form3rxn.str



chain nodes :

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7 8 9 11 12 14 15 18 19 20 21  
ring nodes :  
1 2 3 4 5 6 25 26 27 28 29 30  
ring/chain nodes :  
16 22  
chain bonds :  
1-7 2-15 3-14 5-11 6-12 7-8 7-9 9-16 18-19 18-22 19-20 19-21  
ring bonds :  
1-2 1-6 2-3 3-4 4-5 5-6 25-26 25-30 26-27 27-28 28-29 29-30  
exact/norm bonds :  
1-2 1-6 1-7 2-3 2-15 3-4 3-14 4-5 5-6 5-11 6-12 7-8 7-9 9-16 18-19  
18-22 19-21 25-26 25-30 26-27 27-28 28-29 29-30  
exact bonds :  
19-20  
isolated ring systems :  
containing 1 :

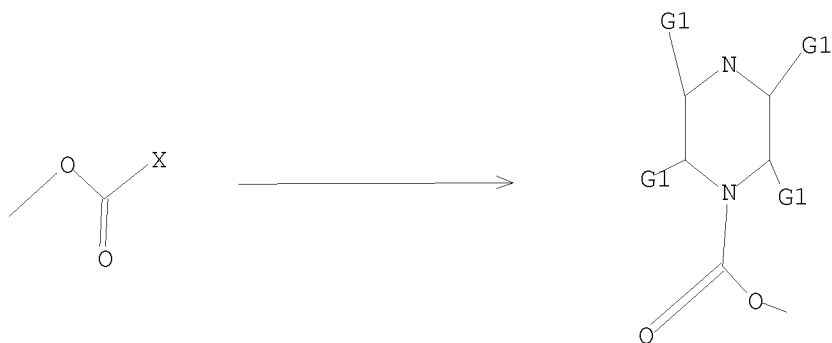
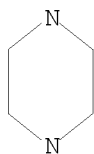
G1:C,H,O,X

Match level :  
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 11:CLASS  
12:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS  
22:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom  
fragments assigned reactant role:  
containing 18  
fragments assigned reagent role:  
containing 25  
fragments assigned product role:  
containing 1

L1 STRUCTURE UPLOADED

=> d 11  
L1 HAS NO ANSWERS  
L1 STR

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G1 C,H,O,X

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

FULL SEARCH INITIATED 11:52:35 FILE 'CASREACT'

SCREENING COMPLETE - 113 REACTIONS TO VERIFY FROM 11 DOCUMENTS

100.0% DONE 113 VERIFIED 9 HIT RXNS 2 DOCS

SEARCH TIME: 00.00.01

L2 2 SEA SSS FUL L1 ( 9 REACTIONS)

=> d ibib abs hit

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L2 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 143:211927 CASREACT

TITLE: Preparation of optically active carbonate intermediates in synthesis of (+)-zopiclone

INVENTOR(S): Bayod Jasanada, Miguel; Sanchez Pedregal, Victor M.; Gotor Santamaria, Vicente; Brieva Collado, M. Rosario; Fernandez Solares, Laura; Diaz Sierra, Monica; Guisan Seijas, Jose Manuel; Paloma Carmona, Jose Miguel; Fernandez-Lafuente, Roberto

PATENT ASSIGNEE(S): Universidad de Oviedo, Spain; Astur Pharma, S.A.

SOURCE: Span., 12 pp.

CODEN: SPXXAD

DOCUMENT TYPE: Patent

LANGUAGE: Spanish

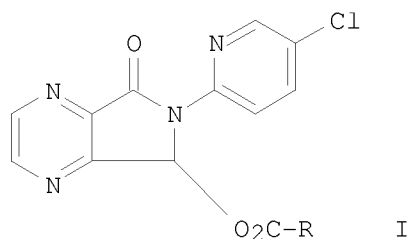
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2203319	A1	20040401	ES 2002-771	20020403
ES 2203319	B1	20050301		
US 6969767	B1	20051129	US 2003-405998	20030402
PRIORITY APPLN. INFO.:			ES 2002-771	20020403

OTHER SOURCE(S): MARPAT 143:211927

GI



AB The invention relates to the synthesis of carbonates I (R = isopropenyloxy, p-nitrophenoxy, chloromethoxy, 1-chloro-, 2-chloro-, 2,2,2-trichloro- or 1,1-dimethyl-2,2,2-trichloroethoxy), their resolution, and use in the synthesis of (+)-zopiclone [(S)-I; R = 4-methyl-1-piperazinyl]. Thus, (S)-I (R = ClCH<sub>2</sub>O) was prepared by esterification of 6-(5-chloro-2-pyridinyl)-5-hydroxy-7-oxo-5,6-dihydropyrrolo[3,4-b]pyrazine with p-nitrophenyl chloroformate and resolution using immobilized lipase B from *Candida antarctica*. Treatment of the product with N-methylpiperazine afforded (+)-zopiclone.

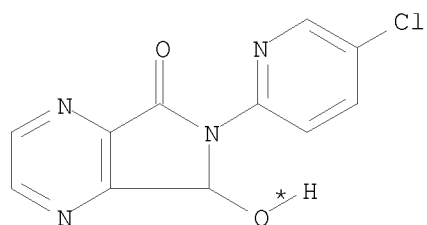
RX(14) OF 14 COMPOSED OF RX(7), RX(9), RX(8)

RX(14) A + P + R ==> T

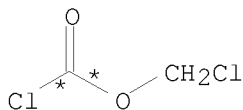
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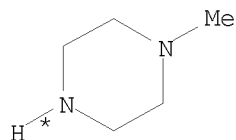
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A

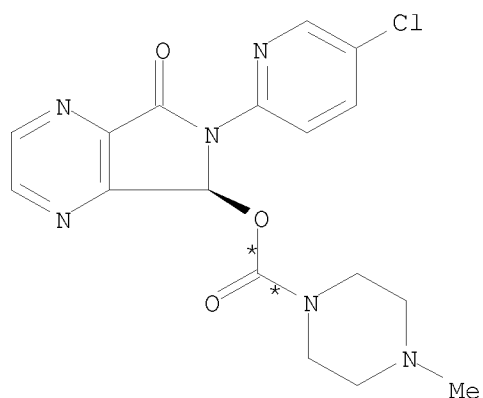


P



R

3  
STEPS  
→



T  
YIELD 90%

RX(7)	RCT	A 43200-81-3, P 22128-62-7
	RGT	D 110-86-1 Pyridine
	PRO	Q 508169-18-4
	SOL	75-09-2 CH2Cl2
	CON	SUBSTAGE(1) 0 deg C
		SUBSTAGE(2) 17 hours, room temperature
RX(9)	RCT	Q 508169-18-4
	RGT	V 290-37-9 Pyrazine
	PRO	S 508169-20-8
	CAT	9001-62-1 Lipase
	SOL	7732-18-5 Water, 108-88-3 PhMe
	CON	100 hours, 60 deg C, pH 7
	NTE	biotransformation, enzymic(immobilized lipase B from Candida antarctica used), buffered solution(phosphate), stereoselective
RX(8)	RCT	R 109-01-3, S 508169-20-8

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PRO T 138729-47-2  
SOL 67-64-1 Me<sub>2</sub>CO  
CON SUBSTAGE(1) 0 deg C  
SUBSTAGE(2) 2 hours, 0 deg C -> 15 deg C

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=> d 12 ibib abs hit 2

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L2 ANSWER 2 OF 2 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 139:307801 CASREACT

TITLE: Stereoselective alkylation of chiral  
2-methyl-4-protected piperazines

INVENTOR(S): Wu, Wenxue; Liao, Hongbiao; Tsai, David J.; Andrews,  
David R.; Gala, Dinesh; Lee, Gary M.; Schwartz, Martin  
Lawrence; McAllister, Timothy L.; Fu, Xiaoyong;  
Maloney, Donal; Thiruvengadam, T. K.; Tann, Chou-Hang

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

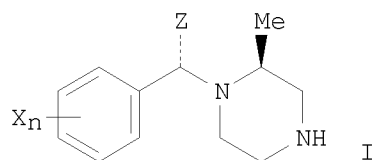
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003084942	A2	20031016	WO 2003-US9275	20030327
WO 2003084942	A3	20040506		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2480481	A1	20031016	CA 2003-2480481	20030327
AU 2003239128	A1	20031020	AU 2003-239128	20030327
US 2003208074	A1	20031106	US 2003-400429	20030327
US 6872826	B2	20050329		
EP 1490346	A2	20041229	EP 2003-733842	20030327
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1642930	A	20050720	CN 2003-807388	20030327
JP 2005526826	T	20050908	JP 2003-582139	20030327
CN 101092401	A	20071226	CN 2007-10140725	20030327
ZA 2004006469	A	20050920	ZA 2004-6469	20040813
MX 2004PA09414	A	20050125	MX 2004-PA9414	20040928
US 2005171120	A1	20050804	US 2005-89858	20050325
PRIORITY APPLN. INFO.:			US 2002-368707P	20020329
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			WO 2003-US9275	20030327

OTHER SOURCE(S): MARPAT 139:307801

GI

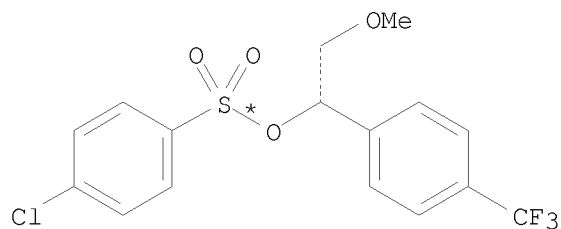
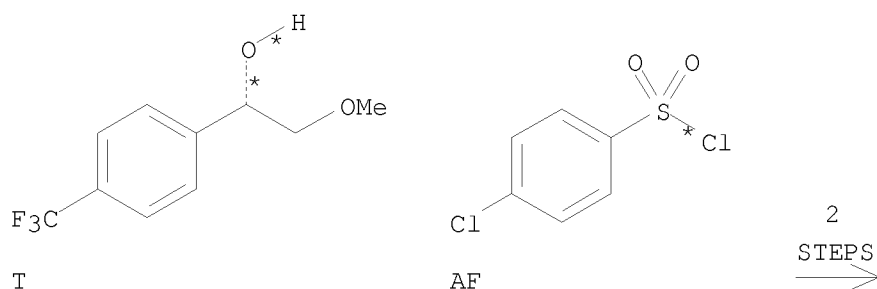
10/513699



AB Chiral 1-substituted-2-methylpiperazines I [X = alkyl, halogen, haloalkyl, alkoxy, aryl, aryloxy, heteroaryl; n = 1-5; Z = alkyl, alkoxyalkyl, aryl, heteroaryl, heteroaralkyl, aralkyl] are prepared by treating 4-protected (S)-2-methylpiperazine with (S)-XnC<sub>6</sub>H<sub>4</sub>CHZ<sub>2</sub>O<sub>3</sub>sY [Y = alkyl, haloalkyl, (un)substituted aryl] and deblocking. Thus, 4-F<sub>3</sub>CC<sub>6</sub>H<sub>4</sub>COCH<sub>2</sub>OMe was reduced to (S)-4-F<sub>3</sub>CC<sub>6</sub>H<sub>4</sub>CH(OH)CH<sub>2</sub>OMe with a chiral borane and converted to (S)-4-F<sub>3</sub>CC<sub>6</sub>H<sub>4</sub>CH(CH<sub>2</sub>OMe)O<sub>3</sub>SC<sub>6</sub>H<sub>4</sub>Cl-4 which was treated with (S)-4-benzyloxycarbonyl-2-methylpiperazine and deblocked to give I [X = 4-F<sub>3</sub>C, Z = CH<sub>2</sub>OMe].

RX(45) OF 104 COMPOSED OF REACTION SEQUENCE RX(10), RX(13)  
AND REACTION SEQUENCE RX(2), RX(13)

...T + AF ==> AG...  
...A + F + AG ==> AM



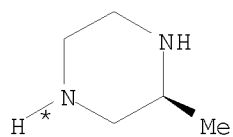
AG

START NEXT REACTION SEQUENCE

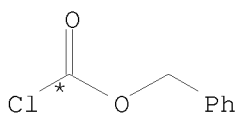
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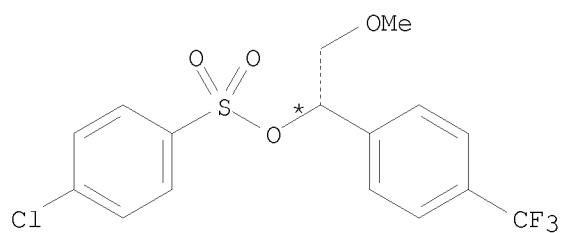
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A

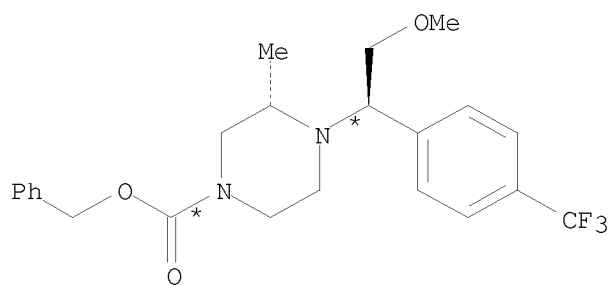


F



AG

2  
STEPS  
→



AM

YIELD 85%

RX(10) RCT T 612493-93-3, AF 98-60-2

STAGE(1)

RGT AH 280-57-9 Triethylenediamine

SOL 108-88-3 PhMe

CON SUBSTAGE(1) 1 hour, -5 - -15 deg C

SUBSTAGE(2) 1 hour, -5 - -15 deg C

STAGE(2)

RGT J 7732-18-5 Water

PRO AG 612493-96-6

RX(2) RCT A 74879-18-8, F 501-53-1

RGT H 64-19-7 AcOH

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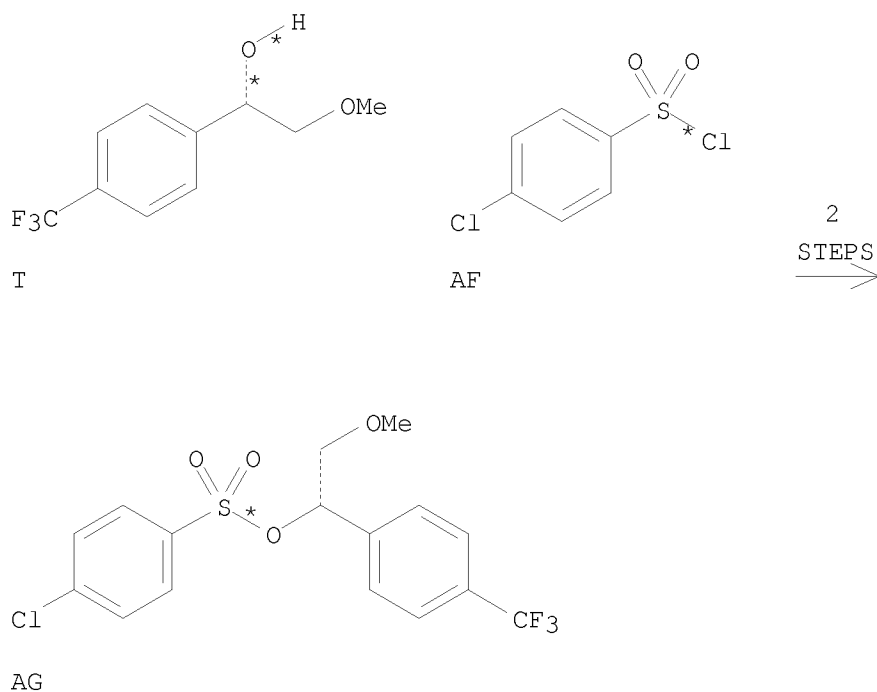
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PRO G 612493-87-5  
SOL 67-56-1 MeOH, 7732-18-5 Water  
CON SUBSTAGE(1) 90 minutes, 0 - 10 deg C  
SUBSTAGE(2) 1 hour, 0 - 10 deg C  
NTE regioselective

RX(13) RCT G 612493-87-5, AG 612493-96-6  
RGT D 584-08-7 K2CO3  
PRO AM 612494-01-6  
SOL 108-88-3 PhMe, 75-05-8 MeCN  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 30 hours, 80 - 85 deg C  
NTE stereoselective, optimization study

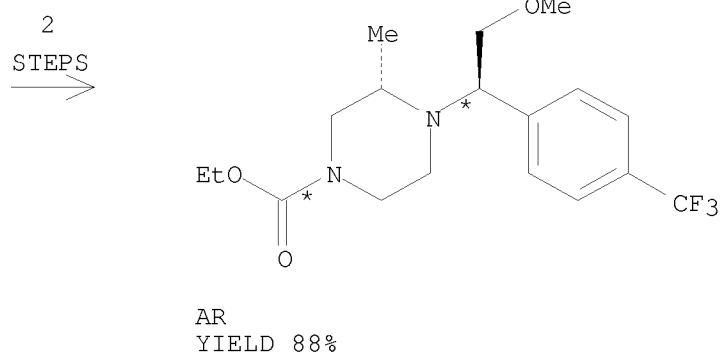
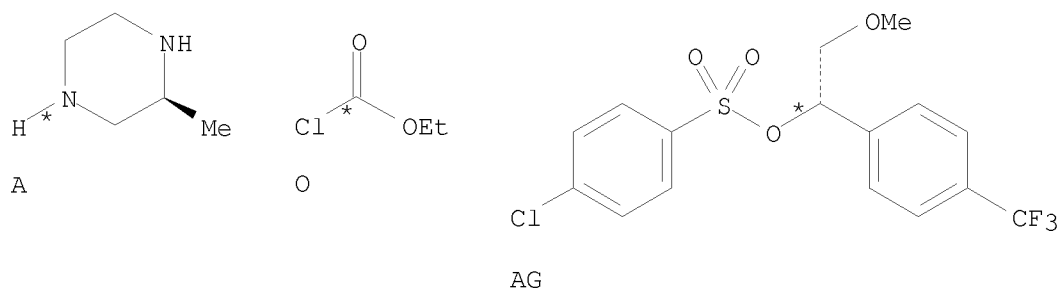
RX(49) OF 104 COMPOSED OF REACTION SEQUENCE RX(10), RX(17)  
AND REACTION SEQUENCE RX(5), RX(17)

...T + AF ==> AG...  
...A + O + AG ==> AR



START NEXT REACTION SEQUENCE

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RX(10) RCT T 612493-93-3, AF 98-60-2

STAGE(1)  
RGT AH 280-57-9 Triethylenediamine  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, -5 - -15 deg C  
SUBSTAGE(2) 1 hour, -5 - -15 deg C

STAGE(2)  
RGT J 7732-18-5 Water

PRO AG 612493-96-6

RX(5) RCT A 74879-18-8, O 541-41-3  
RGT H 64-19-7 AcOH  
PRO P 612493-91-1  
SOL 7732-18-5 Water, 67-56-1 MeOH  
CON SUBSTAGE(1) 90 minutes, 0 - 10 deg C  
SUBSTAGE(2) 1 hour, 0 - 10 deg C  
NTE regioselective

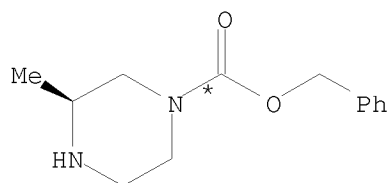
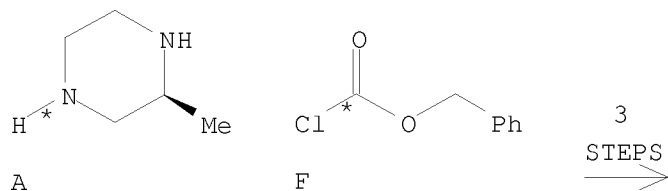
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RGT D 584-08-7 K<sub>2</sub>CO<sub>3</sub>  
PRO AR 612494-06-1  
SOL 108-88-3 PhMe, 75-05-8 MeCN  
CON SUBSTAGE(1) room temperature

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SUBSTAGE(2) 20 hours, 80 - 85 deg C  
NTE stereoselective

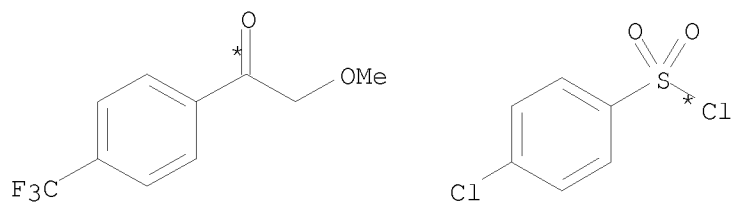
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AND REACTION SEQUENCE RX(7), RX(10), RX(13)

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...S + AF + G ==> AM



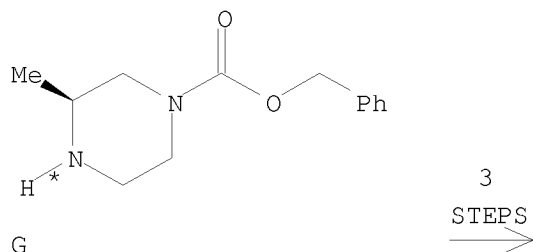
G

START NEXT REACTION SEQUENCE



S

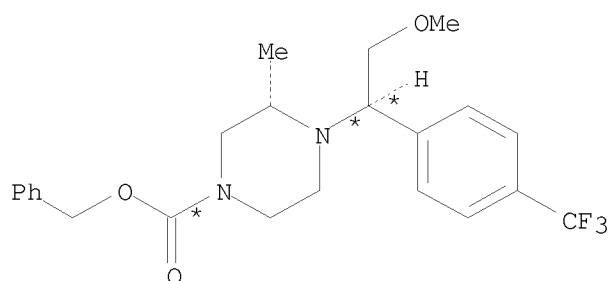
AF



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AM  
YIELD 85%

RX(2) RCT A 74879-18-8, F 501-53-1  
RGT H 64-19-7 AcOH  
PRO G 612493-87-5  
SOL 67-56-1 MeOH, 7732-18-5 Water  
CON SUBSTAGE(1) 90 minutes, 0 - 10 deg C  
SUBSTAGE(2) 1 hour, 0 - 10 deg C  
NTE regioselective

RX(7) RCT S 26771-69-7

STAGE(1)

RGT U 75-75-2 MeSO<sub>3</sub>H, V 14044-65-6 BH<sub>3</sub>-THF  
SOL 109-99-9 THF, 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 10 minutes, room temperature

STAGE(2)

RGT W 112022-81-8 1H,3H-Pyrrolo[1,2-c][1,3,2]oxazaborole,  
tetrahydro-1-methyl-3,3-diphenyl-, (3aS)-  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 30 minutes, room temperature

STAGE(3)

SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, 20 - 30 deg C  
SUBSTAGE(2) 1 hour, room temperature

STAGE(4)

SOL 67-56-1 MeOH  
CON 10 - 20 deg C

PRO T 612493-93-3  
NTE stereoselective

RX(10) RCT T 612493-93-3, AF 98-60-2

STAGE(1)

RGT AH 280-57-9 Triethylenediamine  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, -5 - -15 deg C



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SUBSTAGE(2) 1 hour, -5 - -15 deg C

STAGE(2)

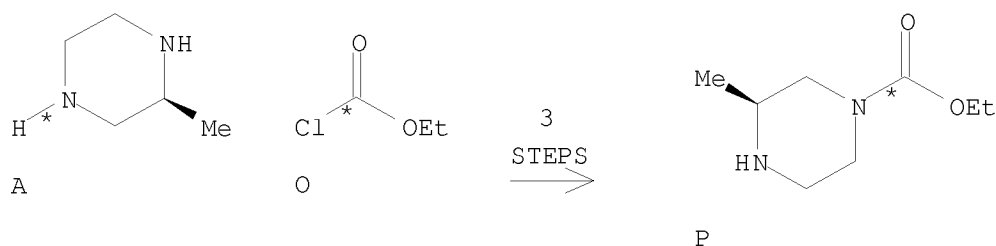
RGT J 7732-18-5 Water

PRO AG 612493-96-6

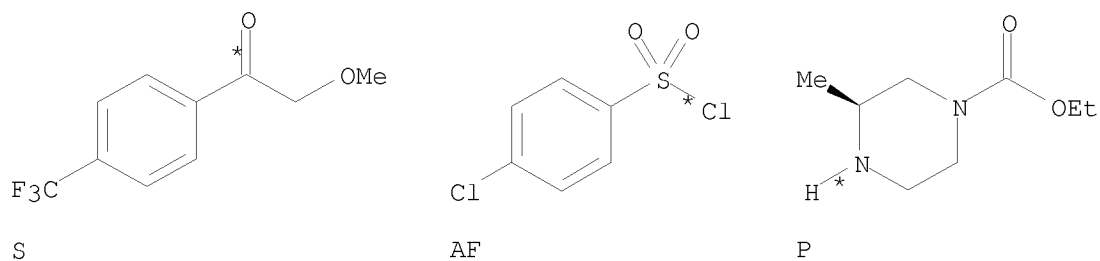
RX(13) RCT G 612493-87-5, AG 612493-96-6  
RGT D 584-08-7 K2CO3  
PRO AM 612494-01-6  
SOL 108-88-3 PhMe, 75-05-8 MeCN  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 30 hours, 80 - 85 deg C  
NTE stereoselective, optimization study

RX(76) OF 104 COMPOSED OF REACTION SEQUENCE RX(5), RX(17)  
AND REACTION SEQUENCE RX(7), RX(10), RX(17)

...A + O ==> P...  
...S + AF + P ==> AR



START NEXT REACTION SEQUENCE

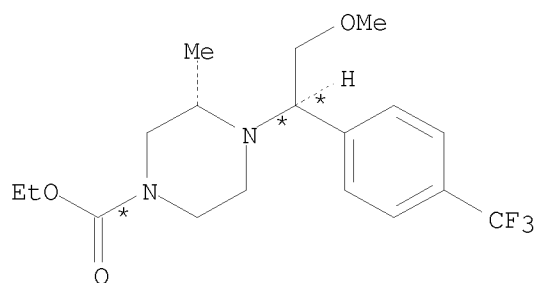


3  
STEPS  
→

<12/04/2007>

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AR  
YIELD 88%

RX(5) RCT A 74879-18-8, O 541-41-3  
RGT H 64-19-7 AcOH  
PRO P 612493-91-1  
SOL 7732-18-5 Water, 67-56-1 MeOH  
CON SUBSTAGE(1) 90 minutes, 0 - 10 deg C  
SUBSTAGE(2) 1 hour, 0 - 10 deg C  
NTE regioselective

RX(7) RCT S 26771-69-7

STAGE(1)

RGT U 75-75-2 MeSO<sub>3</sub>H, V 14044-65-6 BH<sub>3</sub>-THF  
SOL 109-99-9 THF, 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 10 minutes, room temperature

STAGE(2)

RGT W 112022-81-8 1H,3H-Pyrrolo[1,2-c][1,3,2]oxazaborole,  
tetrahydro-1-methyl-3,3-diphenyl-, (3aS)-  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 30 minutes, room temperature

STAGE(3)

SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, 20 - 30 deg C  
SUBSTAGE(2) 1 hour, room temperature

STAGE(4)

SOL 67-56-1 MeOH  
CON 10 - 20 deg C

PRO T 612493-93-3  
NTE stereoselective

RX(10) RCT T 612493-93-3, AF 98-60-2

STAGE(1)

RGT AH 280-57-9 Triethylenediamine  
SOL 108-88-3 PhMe

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CON SUBSTAGE(1) 1 hour, -5 - -15 deg C  
SUBSTAGE(2) 1 hour, -5 - -15 deg C

STAGE(2)

RGT J 7732-18-5 Water

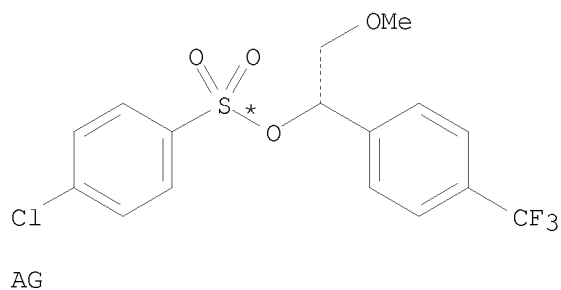
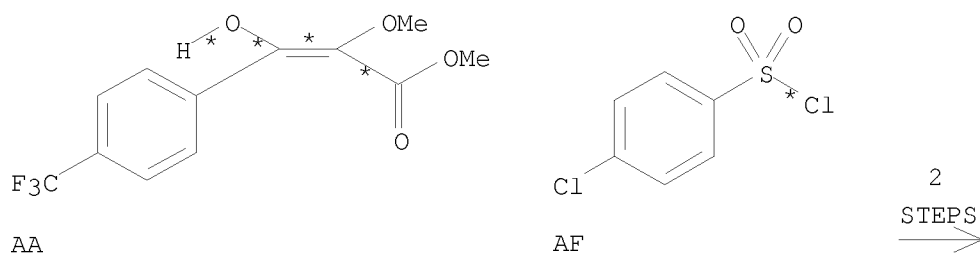
PRO AG 612493-96-6

RX(17) RCT P 612493-91-1, AG 612493-96-6  
RGT D 584-08-7 K2CO3  
PRO AR 612494-06-1  
SOL 108-88-3 PhMe, 75-05-8 MeCN  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 20 hours, 80 - 85 deg C  
NTE stereoselective

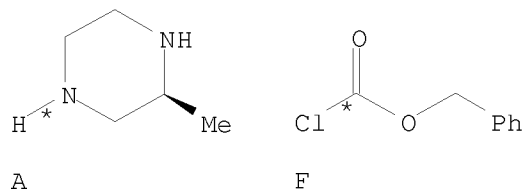
RX(82) OF 104 COMPOSED OF REACTION SEQUENCE RX(9), RX(7), RX(10), RX(13)  
AND REACTION SEQUENCE RX(2), RX(13)

...AA + AF ==> AG...

...A + F + AG ==> AM



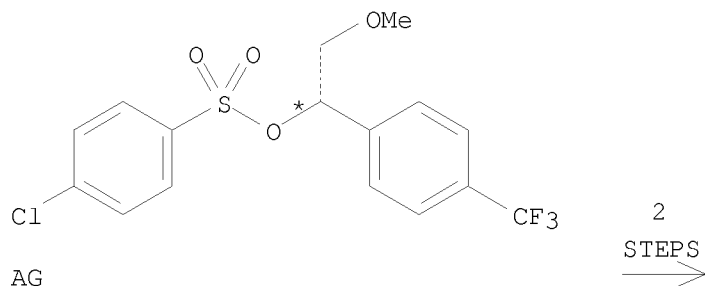
START NEXT REACTION SEQUENCE



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AM  
YIELD 85%

RX(9) RCT AA 612493-95-5  
RGT AC 7664-93-9 H<sub>2</sub>SO<sub>4</sub>  
PRO S 26771-69-7  
SOL 67-56-1 MeOH, 7732-18-5 Water

RX(7) RCT S 26771-69-7

STAGE(1)

RGT U 75-75-2 MeSO<sub>3</sub>H, V 14044-65-6 BH<sub>3</sub>-THF  
SOL 109-99-9 THF, 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 10 minutes, room temperature

STAGE(2)

RGT W 112022-81-8 1H,3H-Pyrrolo[1,2-c][1,3,2]oxazaborole,  
tetrahydro-1-methyl-3,3-diphenyl-, (3aS)-  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 30 minutes, room temperature

STAGE(3)

SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, 20 - 30 deg C  
SUBSTAGE(2) 1 hour, room temperature

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STAGE(4)

SOL 67-56-1 MeOH  
CON 10 - 20 deg C

PRO T 612493-93-3  
NTE stereoselective

RX(10) RCT T 612493-93-3, AF 98-60-2

STAGE(1)

RGT AH 280-57-9 Triethylenediamine  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, -5 - -15 deg C  
SUBSTAGE(2) 1 hour, -5 - -15 deg C

STAGE(2)

RGT J 7732-18-5 Water

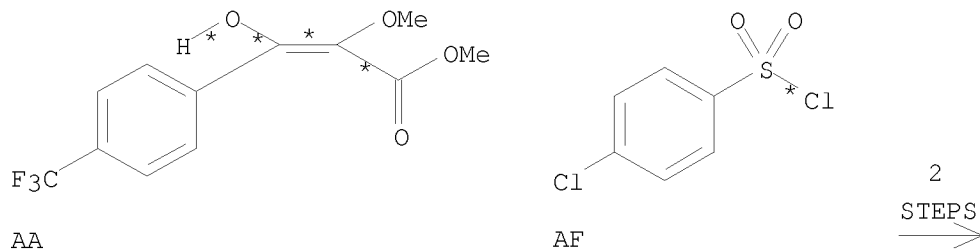
PRO AG 612493-96-6

RX(2) RCT A 74879-18-8, F 501-53-1  
RGT H 64-19-7 AcOH  
PRO G 612493-87-5  
SOL 67-56-1 MeOH, 7732-18-5 Water  
CON SUBSTAGE(1) 90 minutes, 0 - 10 deg C  
SUBSTAGE(2) 1 hour, 0 - 10 deg C  
NTE regioselective

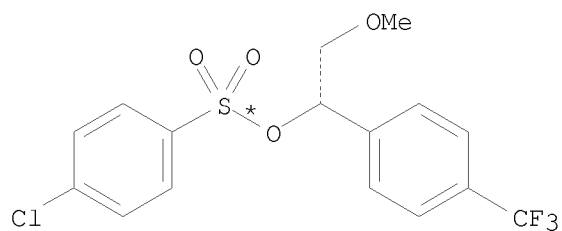
RX(13) RCT G 612493-87-5, AG 612493-96-6  
RGT D 584-08-7 K2CO3  
PRO AM 612494-01-6  
SOL 108-88-3 PhMe, 75-05-8 MeCN  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 30 hours, 80 - 85 deg C  
NTE stereoselective, optimization study

RX(87) OF 104 COMPOSED OF REACTION SEQUENCE RX(9), RX(7), RX(10), RX(17)  
AND REACTION SEQUENCE RX(5), RX(17)

...AA + AF ==> AG...  
...A + O + AG ==> AR

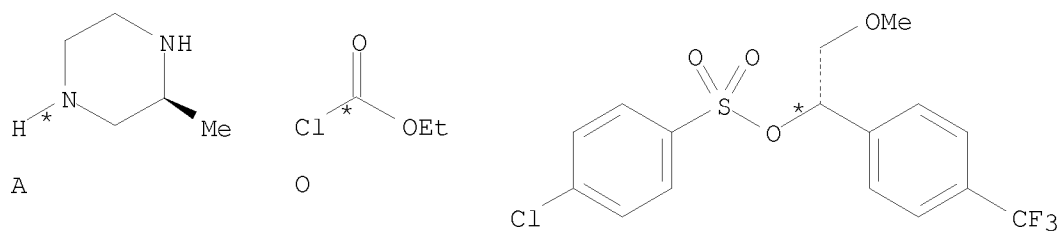


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AG

START NEXT REACTION SEQUENCE

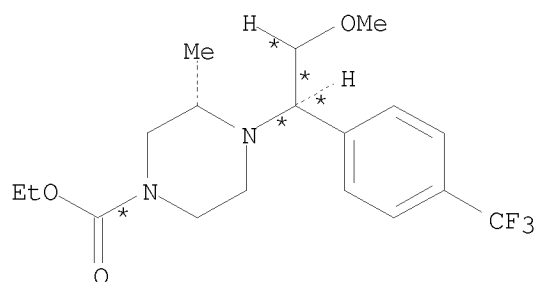


A

O

AG

2  
STEPS  
→



AR

YIELD 88%

RX(9) RCT AA 612493-95-5  
RGT AC 7664-93-9 H2SO4  
PRO S 26771-69-7  
SOL 67-56-1 MeOH, 7732-18-5 Water

RX(7) RCT S 26771-69-7

STAGE(1)

RGT U 75-75-2 MeSO3H, V 14044-65-6 BH3-THF  
SOL 109-99-9 THF, 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 10 minutes, room temperature

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STAGE(2)  
RGT W 112022-81-8 1H,3H-Pyrrolo[1,2-c][1,3,2]oxazaborole,  
tetrahydro-1-methyl-3,3-diphenyl-, (3aS)-  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 30 minutes, room temperature

STAGE(3)  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, 20 - 30 deg C  
SUBSTAGE(2) 1 hour, room temperature

STAGE(4)  
SOL 67-56-1 MeOH  
CON 10 - 20 deg C

PRO T 612493-93-3  
NTE stereoselective

RX(10) RCT T 612493-93-3, AF 98-60-2

STAGE(1)  
RGT AH 280-57-9 Triethylenediamine  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, -5 - -15 deg C  
SUBSTAGE(2) 1 hour, -5 - -15 deg C

STAGE(2)  
RGT J 7732-18-5 Water

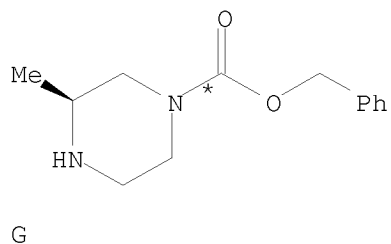
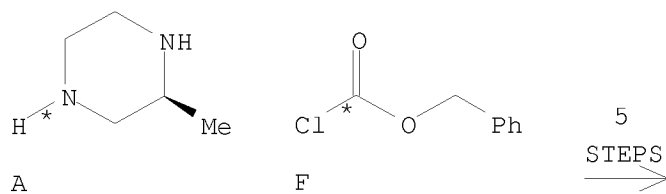
PRO AG 612493-96-6

RX(5) RCT A 74879-18-8, O 541-41-3  
RGT H 64-19-7 AcOH  
PRO P 612493-91-1  
SOL 7732-18-5 Water, 67-56-1 MeOH  
CON SUBSTAGE(1) 90 minutes, 0 - 10 deg C  
SUBSTAGE(2) 1 hour, 0 - 10 deg C  
NTE regioselective

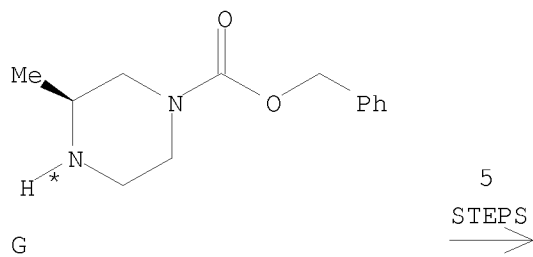
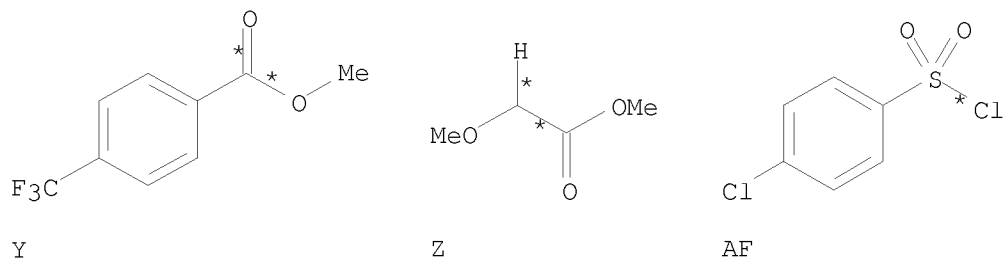
RX(17) RCT P 612493-91-1, AG 612493-96-6  
RGT D 584-08-7 K2CO3  
PRO AR 612494-06-1  
SOL 108-88-3 PhMe, 75-05-8 MeCN  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 20 hours, 80 - 85 deg C  
NTE stereoselective

RX(91) OF 104 COMPOSED OF REACTION SEQUENCE RX(2), RX(13)  
AND REACTION SEQUENCE RX(8), RX(9), RX(7), RX(10), RX(13)  
...A + F ==> G...  
...Y + Z + AF + G ==> AM

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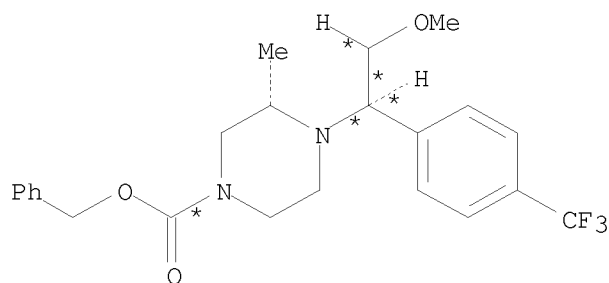


START NEXT REACTION SEQUENCE





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AM  
YIELD 85%

RX(2) RCT A 74879-18-8, F 501-53-1  
RGT H 64-19-7 AcOH  
PRO G 612493-87-5  
SOL 67-56-1 MeOH, 7732-18-5 Water  
CON SUBSTAGE(1) 90 minutes, 0 - 10 deg C  
SUBSTAGE(2) 1 hour, 0 - 10 deg C  
NTE regioselective

RX(8) RCT Y 2967-66-0, Z 6290-49-9

STAGE(1)

RGT AB 124-41-4 NaOMe  
SOL 68-12-2 DMF  
CON SUBSTAGE(1) 5 hours, -10 deg C  
SUBSTAGE(2) 21 hours, -10 deg C

STAGE(2)

RGT AC 7664-93-9 H<sub>2</sub>SO<sub>4</sub>  
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe  
CON -8.5 deg C

PRO AA 612493-95-5  
NTE combined yield of 82%

RX(9) RCT AA 612493-95-5  
RGT AC 7664-93-9 H<sub>2</sub>SO<sub>4</sub>  
PRO S 26771-69-7  
SOL 67-56-1 MeOH, 7732-18-5 Water

RX(7) RCT S 26771-69-7

STAGE(1)

RGT U 75-75-2 MeSO<sub>3</sub>H, V 14044-65-6 BH<sub>3</sub>-THF  
SOL 109-99-9 THF, 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 10 minutes, room temperature

STAGE(2)

RGT W 112022-81-8 1H,3H-Pyrrolo[1,2-c][1,3,2]oxazaborole,  
tetrahydro-1-methyl-3,3-diphenyl-, (3aS)-

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SOL 108-88-3 PhMe  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 30 minutes, room temperature

STAGE(3)  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, 20 - 30 deg C  
SUBSTAGE(2) 1 hour, room temperature

STAGE(4)  
SOL 67-56-1 MeOH  
CON 10 - 20 deg C

PRO T 612493-93-3  
NTE stereoselective

RX(10) RCT T 612493-93-3, AF 98-60-2

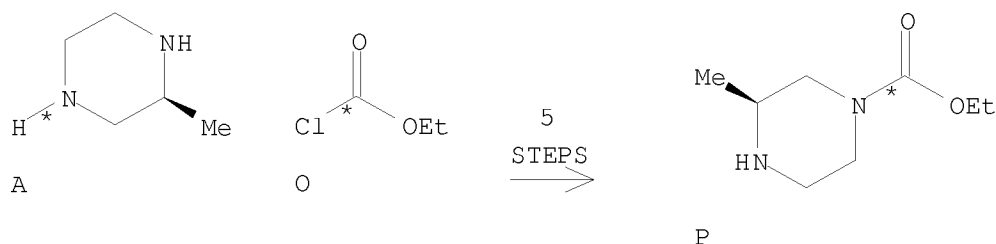
STAGE(1)  
RGT AH 280-57-9 Triethylenediamine  
SOL 108-88-3 PhMe  
CON SUBSTAGE(1) 1 hour, -5 - -15 deg C  
SUBSTAGE(2) 1 hour, -5 - -15 deg C

STAGE(2)  
RGT J 7732-18-5 Water

PRO AG 612493-96-6

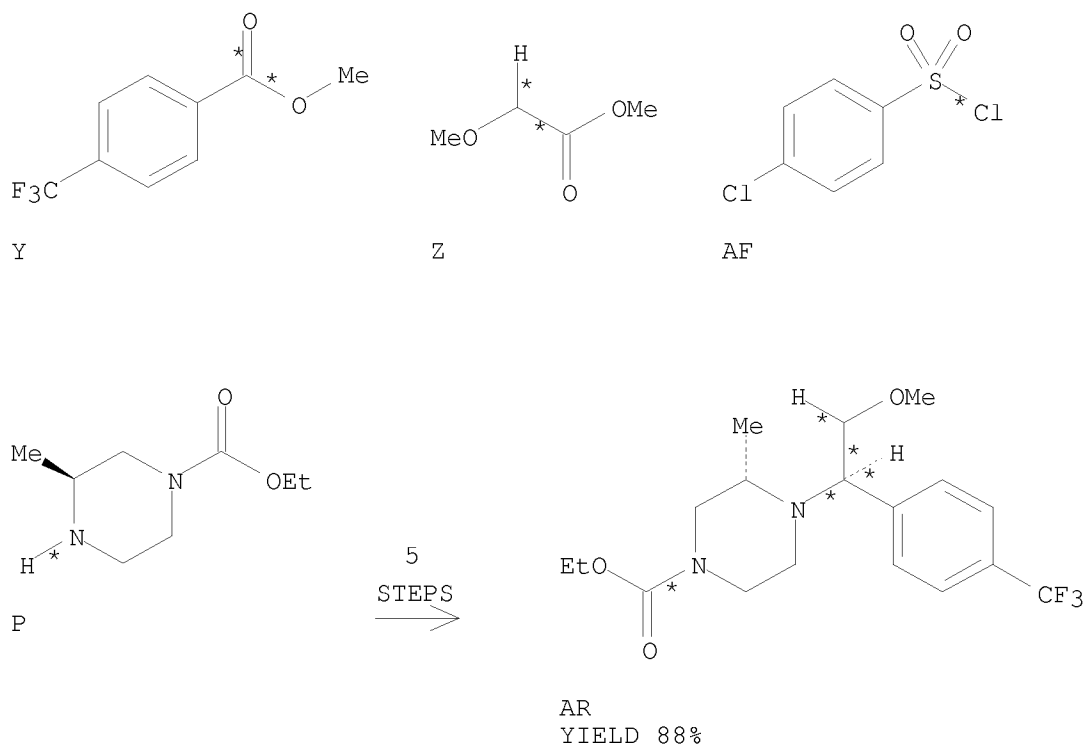
RX(13) RCT G 612493-87-5, AG 612493-96-6  
RGT D 584-08-7 K2CO3  
PRO AM 612494-01-6  
SOL 108-88-3 PhMe, 75-05-8 MeCN  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 30 hours, 80 - 85 deg C  
NTE stereoselective, optimization study

RX(94) OF 104 COMPOSED OF REACTION SEQUENCE RX(5), RX(17)  
AND REACTION SEQUENCE RX(8), RX(9), RX(7), RX(10), RX(17)  
...A + O ==> P...  
...Y + Z + AF + P ==> AR



START NEXT REACTION SEQUENCE

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RX(5) RCT A 74879-18-8, O 541-41-3  
 RGT H 64-19-7 AcOH  
 PRO P 612493-91-1  
 SOL 7732-18-5 Water, 67-56-1 MeOH  
 CON SUBSTAGE(1) 90 minutes, 0 - 10 deg C  
 SUBSTAGE(2) 1 hour, 0 - 10 deg C  
 NTE regioselective

RX(8) RCT Y 2967-66-0, Z 6290-49-9

STAGE(1)

RGT AB 124-41-4 NaOMe  
 SOL 68-12-2 DMF  
 CON SUBSTAGE(1) 5 hours, -10 deg C  
 SUBSTAGE(2) 21 hours, -10 deg C

STAGE(2)

RGT AC 7664-93-9 H2SO4  
 SOL 7732-18-5 Water, 1634-04-4 t-BuOMe  
 CON -8.5 deg C

PRO AA 612493-95-5  
 NTE combined yield of 82%

RX(9) RCT AA 612493-95-5  
 RGT AC 7664-93-9 H2SO4  
 PRO S 26771-69-7

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SOL 67-56-1 MeOH, 7732-18-5 Water

RX(7) RCT S 26771-69-7

STAGE(1)

RGT U 75-75-2 MeSO<sub>3</sub>H, V 14044-65-6 BH<sub>3</sub>-THF

SOL 109-99-9 THF, 108-88-3 PhMe

CON SUBSTAGE(1) room temperature

SUBSTAGE(2) 10 minutes, room temperature

STAGE(2)

RGT W 112022-81-8 1H,3H-Pyrrolo[1,2-c][1,3,2]oxazaborole,  
tetrahydro-1-methyl-3,3-diphenyl-, (3aS)-

SOL 108-88-3 PhMe

CON SUBSTAGE(1) room temperature

SUBSTAGE(2) 30 minutes, room temperature

STAGE(3)

SOL 108-88-3 PhMe

CON SUBSTAGE(1) 1 hour, 20 - 30 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(4)

SOL 67-56-1 MeOH

CON 10 - 20 deg C

PRO T 612493-93-3

NTE stereoselective

RX(10) RCT T 612493-93-3, AF 98-60-2

STAGE(1)

RGT AH 280-57-9 Triethylenediamine

SOL 108-88-3 PhMe

CON SUBSTAGE(1) 1 hour, -5 - -15 deg C

SUBSTAGE(2) 1 hour, -5 - -15 deg C

STAGE(2)

RGT J 7732-18-5 Water

PRO AG 612493-96-6

RX(17) RCT P 612493-91-1, AG 612493-96-6

RGT D 584-08-7 K<sub>2</sub>CO<sub>3</sub>

PRO AR 612494-06-1

SOL 108-88-3 PhMe, 75-05-8 MeCN

CON SUBSTAGE(1) room temperature

SUBSTAGE(2) 20 hours, 80 - 85 deg C

NTE stereoselective

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(FILE 'HOME' ENTERED AT 11:52:01 ON 01 FEB 2008)

FILE 'REGISTRY' ENTERED AT 11:52:06 ON 01 FEB 2008

FILE 'CASREACT' ENTERED AT 11:52:10 ON 01 FEB 2008

L1 STRUCTURE UPLOADED

L2 2 S L1 FULL

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

132.70

133.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-1.50

-1.50

STN INTERNATIONAL LOGOFF AT 11:53:55 ON 01 FEB 2008